III. REMARKS

Claims 1-4 are under consideration in this application. Claims 5-13 are held withdrawn from consideration as being drawn to nonelected subject matter 37 CFR 1.142(b). Claims 1-4 have been amended.

Claim Rejections* - 35 *USC § 102

Claims 1-4 stand rejected under 35 U.S.C. 102(a) and/or (b) as being anticipated by Hashimoto et al. (CA 136:59990) and Kotar-Jordan et al. (The Second Central, etc., 1997, pages 228-229).

The examiner states that Hashimoto et. at. and Kotar-Jordan et at. specifically disclose the instant compounds referring to RN 103577 of Hashimoto et al or page 289 of Kotar-Jordan et at. Hence, the instant compound is deemed anticipated therefrom.

Applicant respectfully disagrees.

Both of the above identified references disclose the specific compound 2 -[[3-methyl-4-(2 ,2 ,2 -trifluoroethoxy)- 2 - pyridyl]methyl]- sulfinyl]benzimidazole (compound 1) in forms where the compound may also contain water.

However, that particular compound is not encompassed by the structural formula I of the presently claimed compounds because the substituents R1 R2 and R3 cannot represent a trifuoroalkoxy-moiety. In particular, the alkoxy substituent itself cannot be substituted with fluorine, so that the definition also does not encompass the respective (2,2,2)-trifluoroethoxy group in the above identified compound 1.

Consequently, the presently claimed invention is novel in view of the cited prior art.

Claim* Rejections - 35 *USC 103

Claims 1-4 stand rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Hashimoto et at. and Kotar-Jordan et al. in view of Brittain et al. (Polymorphism in Pharmaceutical Solids, NY: Marcel Dekker, Inc., 1999, pages 125-181,279-330).

The examiner states that Hashimoto et at. and Kotar-Jordan et al. teach the crystal forms of the instant known compounds, citing, for example, page 289 of Kotar-Jordan et al. and further states that Brittain et al. teach that at any particular temperature and pressure, only one crystalline form is thermodynamically stable.

The examiner concludes that the claimed crystalline form as well as its relative selectivity of properties *vis-a-vis* the known compound are suggested by the references and that it would appear obvious to one skilled in the art in view of the references that the instant compound would exist in different crystalline forms. No unexpected or unobvious properties are noted by the examiner.

Applicants respectfully disagree.

As set forth above, the reference of Hashimoto et al. discloses the compound 2 -[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]-sulfinyl]benzimidazole (M = 353 g/mol, compound 1), which is not encompassed by the structural formula I of the presently claimed compounds.

In addition, the reference of Hashimoto et al. does not disclose that compound 1 is obtained in form of hydrates. The term hydrates refers to compounds wherein water molecules are bonded

via intermolecular forces, in particular via hydrogen bonds. The mere declaration of a water content of 1.89 % does not indicate the presence of hydrates as water may also be present in a compound in unbound form, e. g. as residual water or in form of clathrates.

As neither the compounds of the present invention nor hydrates of said compounds are mentioned in the reference of Hashimoto et al. that reference does not give any hint to those skilled in the art of how to prepare the inventively claimed hydrates.

The reference of Kotar-Jordan et al. also discloses compound 1. According to Kotar-Jordan et al. the compound may be present in form of a monohydrate which is itself present in the form of two polymorphs and more solvates.

The reference of Kotar-Jordan et al. discloses compounds that are different in molecular structure and physical properties than the compounds of the present invention.

In particular, the absence of a fluoroalkoxy moiety leads to different physical properties, for example a different polarity. Therefore, it is surprising and inventive that hydrates of the compounds of general formula I according to the present invention can be obtained.

Moreover, the reference by Kotar-Jordan et al. does not disclose a general process which would allow those skilled in the art to prepare crystals of hydrates of optionally substituted 2-(2-pyridinyl)methylthio-1 H-benzimidazoles of general formula I. This reference merely discloses a process for recrystallization of compound 1 from various solvents with the addition of water at different ranges of temperatures to obtain a monohydrate of

compound 1, which is present in the form of two polymorphs and more solvates. Neither the exact amount of water nor the exact range of temperature is given. In addition, the reference neither describes further substituted 2-(2-pyridinyl)methylthio-1 H-benzimidazoles of general formula I besides compound 1 nor does it describe crystalline hydrates thereof different than monohydrates.

Therefore, it is also surprising and inventive in view of the teachings from Kotar-Jordan et al. that substituted 2-(2-pyridinyl)methylthio-1H-benzimidazoles which contain 0.5 to 2 mol water per mol of substituted 2-(2-pyridinyl)methylthio-1H-benzimidazoles of general formula I can be obtained in the form of crystals.

***Claim Rejections* - 35 *USC* 112, first paragraph**

Claims 1-4 stand rejected under 35 U.S,C. 112, first paragraph, as failing to comply with the written description requirement because the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention in that there is a lack of description as to whether the instant hydrates are maintained upon storage.

The examiner states that substances may hydrate/dehydrate in response to changes in environmental conditions such as where processing a compound into a pharmaceutical composition could dehydrate or create a different hydrate than the hydrates being claimed or even back to the compound itself. Citing page 127 of Brittain, the examiner states that changes in hydration state can result in variable potencies depending on handling

conditions during weighing steps, the kinetics of the hydration process, and the environmental conditions during processing.

The examiner states that there is no description as to how applicants produced and isolated the particular hydrates being claimed and that applicants have failed to show how each hydrate is isolated. The examiner cites page 281 of Brittain or page 1843 of U.S. Pharmacopia) for the proposition that only when water is incorporated into the crystal lattice of the compound in stoichiometric proportions, are particular hydrates formed.

The examiner further states that the specification fails to describe the compounds in terms of their powder X-ray diffraction pattern or infrared spectrum data or how the crystalline forms will be maintained and prevented from converting to other forms.

The examiner concludes that the specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation, citing In re Fouche,169 USPQ 429 CCPA 1971, MPEP 716.02(b).

Applicants respectfully disagree.

The preparation of crystals of hydrates of substituted 2-(2-pyridinyl)methylthio-1 H- benzimidazoles of general formula I is described in detail in examples 1 to 4 of the present application. In particular, the amount of water needed, the exact temperature range and methods to isolate said crystals are stated explicitly.

The existence of substituted 2-(2-pyridinyl)methylthio-1 H-benzimidazoles of general formula I is demonstrated by the HPLC experiments described in the specification.

Moreover, applicants provide further evidence that hydrates of substituted 2-(2-pyridinyl)methylthio-1 H-benzimidazoles of general formula I are indeed obtained by submitting a signed declaration of Dr. Helmut Lobermann.

Pyrmetazol, which was obtained according to the process described in the present application, was dried using a halogen dehumidifier until a constant weight was maintained. The water content of the dry pyrmetazol was determined *to* be about 4.8 % (equivalent to x being 1.14). The recorded infrared spectra showed the presence of water (absorbance between 3600 - 3100 cm^{-1} and at about 1620 cm^{-1}). Therefore, the water molecules that are present in pyrmetazol are bonded to pyrmetazol molecules via hydrogen bonds. Consequently, pyrmetazol is evidently obtained in form of hydrates.

In summary, a person skilled in the art can carry out the present invention on the basis of the present description as is and is also supported by the declaration of Dr. Lobermann.

Claim Rejections - 35 USC 112, second paragraph

Claims 1-4 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention in that claims 1-4 is indefinite what is meant by residue

The term "residue" in claims 1 to 4 has been replaced with the term "moiety" which is a more exact translation in this context

of the German word "Rest" that can be found in the originally filed PCT application.

The examiner states that the plural's' on "compounds" and "compositions" makes claims 1-4 read on mixtures rather than specific compounds.

Applicants cannot find the terms "compounds" and "compositions" in claims 1 to 4. In case these terms have been confused with "crystals" and "hydrates" these terms have been converted to the respective singular forms.

Applicant assumes that the Examiner's objections with respect to the patentability of the present invention will be overcome by the argumentation and/or amendments presented above.

A check is enclosed for the three-month extension of time fee. The Commissioner is hereby authorized to charge payment for any fees associated with this communication or credit any over payment to Deposit Account No. 16-1350.

Respectfully submitted,

December 15, 2005
Date

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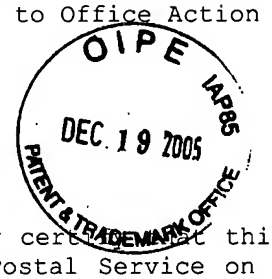

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